Remarks

New claims 13-19 have been added. The new claims are supported by the original claims 1-7 and the specification at pages 2-4. Claims 1-7 and 9-19 are now pending. Claims 9-12 have been withdrawn from consideration by the Examiner.

Information Disclosure Statement

The two search reports that were not considered by the Examiner due to lack of a date on SB08 form have been resubmitted in a proper format together with appropriated fees and certification. Reconsideration is respectfully requested.

Title

The title has been amended to meet the requirements.

35 U.S.C. §112, First Paragraph

In the Office Action, claims 1-7 were rejected under 35 U.S.C. §112, first paragraph for not enabling a method of inhibiting cathepsin S in warm blooded animals nor enablement for the making of the active agent of the claimed invention. Applicants respectfully traverse this rejection for the reasons stated below.

Applicants respectfully submit that the instant application teaches a skilled person the method of inhibiting cathepsin S in warm blooded animals using claimed compounds without undue experimentation.

As the Examiner has accurately stated, the factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount of direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. To make a proper rejection all these factors must be analyzed and any conclusion of nonenablement must be based on the evidence as a whole. See MPEP §2164.01(b).

In the Office Action, the Examiner listed a number of reasons/*Wands* factors to support the rejection. Applicants respectfully respond to each of these reasons/*Wands* factors as follows.

In the Office Action, the Examiner averred that Applicants did not identify patients, predict dosages and routes of administration. To the contrary, Applicants described the routes of administration (see lines 16-22, page 7 of the specification), and dosages (see lines 31, page 7 to lines 2, page 8; further on page 9). Furthermore, Applicants identify the potentially suitable patients that can benefit from one or more of the compounds (see lines 19-26, page 6).

The Examiner further stated that the invention was not enabled because of "no indication of any commonality of mechanism of action for the recited drug." See Office Action, Page 4. Applicants clearly stated in the specification that the compounds of the invention produce "inhibition of a cysteine protease in a warm blooded animal." See line 20, page 6 of the Specification. Furthermore, understanding the mechanism of action is not even required for enablement purposes. In fact, the Federal Circuit held in *Fromson v. Advance Offset Plate, Inc.*, that an inventor's theory and belief about how his invention operates is unnecessary to meet the enablement requirement of §112, and that an inventor "need not comprehend the scientific principles on which the practical effectiveness of his invention rests." *Fromson v. Advance Offset Plate, Inc.*, 720 F.2d 1565, 1570, 219 U.S.P.Q. 1137, 1140 (Fed. Cir. 1983).

The Examiner also alleged that "[n]one of the examples either singl[y] or collectively demonstrate each of the treatments as successful" without providing any objective evidences. According to MPEP §2164.04, the Examiner bears the initial burden to come forward with evidence to establish a reasonable basis to question the enablement provided for the claimed invention. See MPEP §2164.04. Furthermore, the instant Application describes an *In Vitro* assay to test the effectiveness of these compounds. See Line 26, Page 18 to Line 7, Page 19 of the instant Application. It would not require undue experimentation to test these compounds using the assay provided in the instant Specification to demonstrate the efficacy of these compounds.

The Examiner further alleged: "the Specification does not provide any guidance in terms of any pharmaceutical indication." To the contrary, the Specification provides detailed pharmaceutical indications at Lines 24-26, page 6.

The Examiner further alleged: "[t]he specification does not provide any guidance in terms of inhibiting cathepsin S." Again, Applicants respectfully submit that an *In Vitro* assay

is provided in the Specification to measurement a compound's activities toward Cathepsin S. See Line 26, Page 18 to Line 7, Page 19.

The Examiner further used the rationale that "since the compounds are novel, there is a lack of predictability." If there is the standard, all patented inventions would be considered unpredictable, because all of the patented inventions would be arguably "novel." Even if the instant field of technology is considered "unpredictable," Applicants believe that the Specification provides numerous Examples (a total of 9) to enable the entire scope as claimed.

Finally, the Examiner argued that "the starting material… (3aR,7aR)-hexahydro[-2-benzofuran-1,3-dione] is a critical source compound and the Specification does not provide sufficient enablement to make the invention." Applicants respectfully submit that (3aR,7aR)-hexahydro-2-benzofuran-1,3-dione is also known as "(-)-trans-1,2-cyclohexanedicarboxylic anhydride," which was a known compound in literature when the instant application was filed. For example, a reference published in year 2000 described the synthesis of this compound. See Tetrahedron, 56 (2000) 3309-3318, more specifically at page 3312, Compound No 12, and Experimental at page 3315, the 1st compound described. A copy of this reference is cited in the Information Disclosure Statement filed together with this response. Therefore, Applicants submit that the pending claims are enabled for this additional reason.

Having discussed all the *Wands* factors presented by Examiner, Applicants submit that viewing these factors as a whole would lead one to conclude that the pending claims 1-7 are enabled. Withdraw of this rejection is respectfully requested.

Furthermore, the pending claim 7 claims only the method of inhibiting Cathepsin S using a compound selected from the list of compounds and pharmaceutically acceptable salts thereof. Therefore, claim 7 is a narrower claim than claim 1-6. The "breath of claim" *Wands* factor further favors the enablement of claim 7 in addition to those reasons described above. Withdraw of this rejection as being applied to claim 7 is respectfully requested for this additional reason.

These arguments are also applicable to the new claims 13-19. Therefore, claims 13-19 are enabled and, thus, patentable.

Having responded all the rejections, Applicants believe the pending claims are in condition for allowance and a speedy office so indicating is respectfully requested.

Respectfully submitted,

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The Commissioner for Patents is hereby authorized to charge payment to Deposit Account No. **26-0166** for any fees associated with this communication.